

L Number	Hits	Search Text	DB	Time stamp
1	1918	(514/220,291,411).CCLS.	USPAT; US-PGPUB	2003/08/05 15:27
2	134	(540/586).CCLS.	USPAT; US-PGPUB	2003/08/05 15:27
3	235	(546/90).CCLS.	USPAT; US-PGPUB	2003/08/05 15:27
4	162	(548/430).CCLS.	USPAT; US-PGPUB	2003/08/05 15:27
5	2314	((514/220,291,411).CCLS.) ((540/586).CCLS.) ((546/90).CCLS.) ((548/430).CCLS.)	USPAT; US-PGPUB	2003/08/05 15:28
6	0	((514/220,291,411).CCLS.) ((540/586).CCLS.) ((546/90).CCLS.) ((548/430).CCLS.)) AND (lipoperoxide OR (lipid ADJ peroxida?))	USPAT; US-PGPUB	2003/08/05 15:28
7	0	((514/220,291,411).CCLS.) ((540/586).CCLS.) ((546/90).CCLS.) ((548/430).CCLS.)) AND ("furo[2,3-f]" OR "furo(2,3-f)" OR (furo ADJ "2,3-f"))	USPAT; US-PGPUB	2003/08/05 15:30

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask.CAS" for self-help around the clock
NEWS	3	Feb 24	PCTGEN now available on STN
NEWS	4	Feb 24	TEMA now available on STN
NEWS	5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	6	Feb 26	PCTFULL now contains images
NEWS	7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS	8	Mar 24	PATDPAFULL now available on STN
NEWS	9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS	10	Apr 11	Display formats in DGENE enhanced
NEWS	11	Apr 14	MEDLINE Reload
NEWS	12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS	13	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS	14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS	15	Apr 28	RDISCLOSURE now available on STN
NEWS	16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS	17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS	18	May 15	Supporter information for ENCOMPAT and ENCOMPLIT updated
NEWS	19	May 19	Simultaneous left and right truncation added to WSCA
NEWS	20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS	21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS	22	Jun 06	PASCAL enhanced with additional data
NEWS	23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS	24	Jun 25	HSDB has been reloaded
NEWS	25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS	26	Jul 21	Identification of STN records implemented
NEWS	27	Jul 21	Polymer class term count added to REGISTRY
NEWS	28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS EXPRESS			April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS INTER			General Internet Information
NEWS LOGIN			Welcome Banner and News Items
NEWS PHONE			Direct Dial and Telecommunication Network Access to STN
NEWS WWW			CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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***** STN Columbus *****

FILE 'HOME' ENTERED AT 11:04:29 ON 05 AUG 2003

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.42

0.42

FILE 'REGISTRY' ENTERED AT 11:05:26 ON 05 AUG 2003

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STRUCTURE FILE UPDATES: 4 AUG 2003 HIGHEST RN 560991-54-0

DICTIONARY FILE UPDATES: 4 AUG 2003 HIGHEST RN 560991-54-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

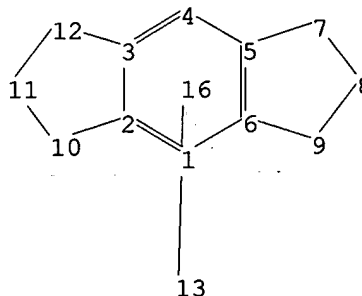
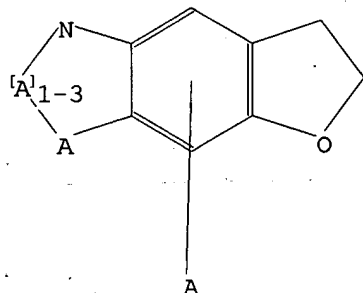
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading C:\Program Files\Stnexp\Queries\10069180.str



chain nodes :

13

10/069,180Thomas McKenzie

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12

ring bonds :

1-2 1-6 2-3 2-10 3-4 3-12 4-5 5-6 5-7 6-9 7-8 8-9 10-11 11-12

exact/norm bonds :

2-10 3-12 5-7 6-9 10-11 11-12

exact bonds :

7-8 8-9

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 16:CLASS

L1 STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 11:05:42 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 10453 TO ITERATE

9.6% PROCESSED 1000 ITERATIONS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 202938 TO 215182

PROJECTED ANSWERS: 16 TO 402

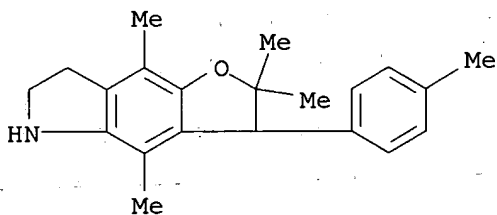
L2 1 SEA SSS SAM L1

=> d scan

L2 1 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN

IN 2H-Furo[2,3-f]indole, 3,5,6,7-tetrahydro-2,2,4,8-tetramethyl-3-(4-methylphenyl)- (9CI)

MF C21 H25 N O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10/069,180Thomas McKenzie

ALL ANSWERS HAVE BEEN SCANNED

=> s l1 full

FULL SEARCH INITIATED 11:06:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 206535 TO ITERATE

100.0% PROCESSED 206535 ITERATIONS
SEARCH TIME: 00.00.03

32 ANSWERS

L3 32 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

148.55

148.97

FILE 'CAPLUS' ENTERED AT 11:06:42 ON 05 AUG 2003
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FILE COVERS 1907 - 5 Aug 2003 VOL 139 ISS 6
FILE LAST UPDATED: 4 Aug 2003 (20030804/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 7 L3

=> s wo2001014384?/pn

L5 1 WO2001014384?/PN
(WO2001014384/PN)

=> s l4 not l5

L6 6 L4 NOT L5

=> d 1-6 cbib pi abs hitstr

L6 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
2002:456563 Document No. 137:262696 The silver nitrate oxidation of
2,2,4,6,7-pentamethylcoumaran-5-ol. Schadel, Uta; Gruner, Margit;
Habicher, Wolf D. (Institute of Organic Chemistry, Dresden University of
Technology, Dresden, 01069, Germany). Tetrahedron, 58(25), 5081-5086
(English) 2002. CODEN: TETRAB. ISSN: 0040-4020. Publisher: Elsevier

Science Ltd..

AB The silver nitrate oxidation of 2,2,4,6,7-pentamethylcoumaran-5-ol was investigated. The complex mixture of products formed is in partial disagreement with the mechanisms supposed so far and suggests a less strong Mills-Nixon effect than assumed until now. Consecutive reactions of 2,2,4,7-tetramethylcoumaran-5,6-dione, which was formed as main product, were examined

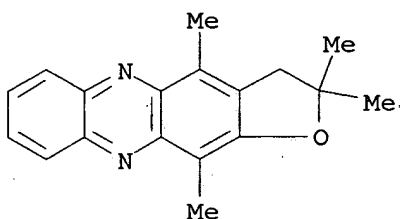
IT 462092-02-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(mechanism of silver nitrate oxidation of 2,2,4,6,7-pentamethylcoumaran-5-ol and further reactions of 2,2,4,7-tetramethylcoumaran-5,6-dione as its main oxidation product)

RN 462092-02-0 CAPLUS

CN Furo[2,3-b]phenazine, 2,3-dihydro-2,2,4,11-tetramethyl- (9CI) (CA INDEX NAME)

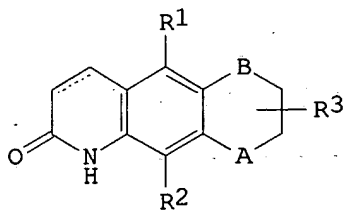


L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

1994:298644 Document No. 120:298644 Preparation of furo- or pyranoquinoline derivatives or their salts as cardiotonics, antiarrhythmics, and vasodilators. Kyotani, Yoshinori; Taima, Tsutomu; Kurihara, Juji; Kitamura, Takahiro; Kama, Kazuhiro; Yamaguchi, Takashi; Onoki, Kazuhiro; Sato, Seiichi; Oota, Tomio; Uchida, Yasuyoshi (Kowa Co, Japan). Jpn. Kokai Tokkyo Koho JP 05339271 A2 19931221 Heisei, 14 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1992-145545 19920605.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05339271	A2	19931221	JP 1992-145545	19920605
JP 3153335	B2	20010409		

GI



I

AB The title derivs. I [R1-2 = H, lower alkyl; R3 = (un)substituted lower alkyl, lower alkanoyloxy, OH, lower alkylsulfonyloxy, azido, amino; A = O, direct bond; when A = O then B = direct bond or CH:CH; when A = direct

bond then B = O] or their salts are prepared as cardiotonics, antiarrhythmics, and vasodilators (no data). A solution of 7-acetoxy-1,2-dihydro-6-(2,3-epoxypropyl)-8-methylquinolin-8-one (preparation from 3-amino-o-cresol in 6 steps) in DMF was treated with aqueous NaOH at 50° for 30 min to give 61.8% 2-hydroxymethyl-9-methyl-2,3,7,8-tetrahydrofuro[3,2-g]quinolin-7-one.

IT 154521-24-1P 154521-25-2P 154521-26-3P

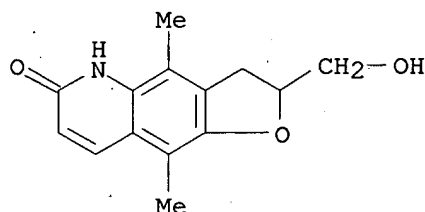
154521-27-4P 154521-28-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as cardiotonic and antiarrhythmic and vasodilator)

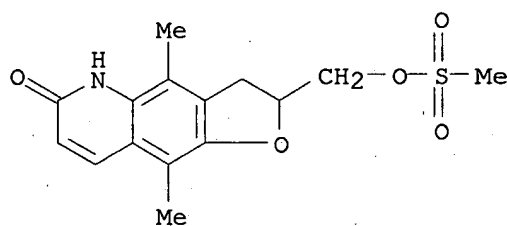
RN 154521-24-1 CAPLUS

CN Furo[2,3-g]quinolin-6(5H)-one, 2,3-dihydro-2-(hydroxymethyl)-4,9-dimethyl- (9CI) (CA INDEX NAME)



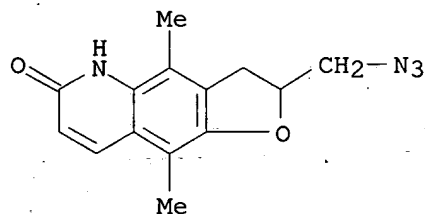
RN 154521-25-2 CAPLUS

CN Furo[2,3-g]quinolin-6(5H)-one, 2,3-dihydro-4,9-dimethyl-2-[(methanesulfonyl)oxy]methyl- (9CI) (CA INDEX NAME)



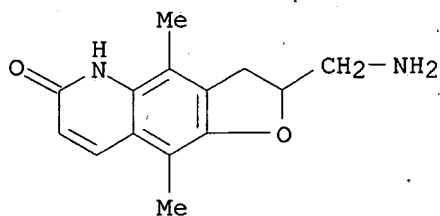
RN 154521-26-3 CAPLUS

CN Furo[2,3-g]quinolin-6(5H)-one, 2-(azidomethyl)-2,3-dihydro-4,9-dimethyl- (9CI) (CA INDEX NAME)



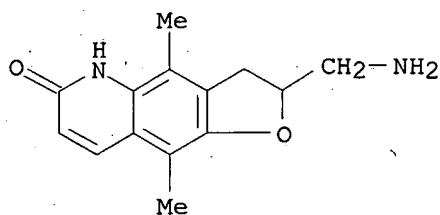
RN 154521-27-4 CAPLUS

CN Furo[2,3-g]quinolin-6(5H)-one, 2-(aminomethyl)-2,3-dihydro-4,9-dimethyl- (9CI) (CA INDEX NAME)



RN 154521-28-5 CAPLUS

CN Furo[2,3-g]quinolin-6(5H)-one, 2-(aminomethyl)-2,3-dihydro-4,9-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

1993:230163 Document No. 118:230163 Studies on the constituents of *Aristolochia liukiuensis*. II. Kazuhito, Ogiwara; Zhao, Jiaping; Higa, Matsutake; Yogi, Seiichi (Coll. Sci., Univ. Ryukyus, Nishihara, 903-01, Japan). Bulletin of the College of Science, University of the Ryukyus, 54, 17-28 (Japanese) 1992. CODEN: BCSRZD. ISSN: 0286-9640.

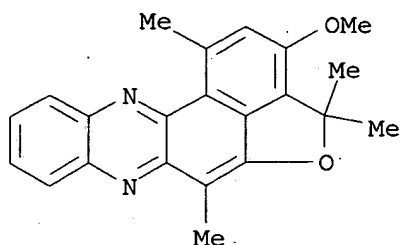
AB The root of *Aristolochia liukiuensis* contained aristolactone, mansonone G, dehydrooxoperezinone, aristololactam DII, 3,4-methylenedioxy-8-methoxyphenanthrene-1-carboxylic acid, aristolochic acid II, and aristolochic acid IV Me ester.

IT 18142-22-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

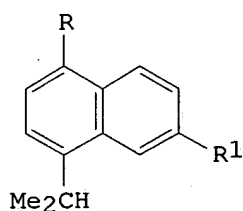
RN 18142-22-8 CAPLUS

CN 4H-Isobenzofuro[7,1-ab]phenazine, 3-methoxy-1,4,4,6-tetramethyl- (8CI, 9CI) (CA INDEX NAME)

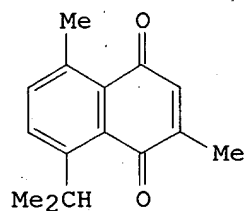


L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
 1987:18852 Document No. 106:18852 Oxygenation of cadalene and eudalene in
 polar aprotic solvents. Takekuma, Shinichi; Matsubara, Yoshiharu;
 Yamamoto, Hiroshi; Nozoe, Tetsuo (Fac. Sci. Technol., Kinki Univ.,
 Higashi-Osaka, Japan). Yukagaku, 34(12), 1026-8 (English) 1985. CODEN:
 YK GKAM. ISSN: 0513-398X. OTHER SOURCES: CASREACT 106:18852.

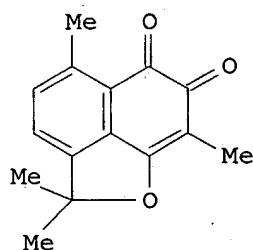
GI



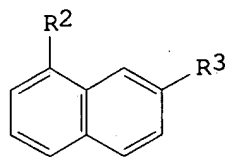
I



II



III



IV

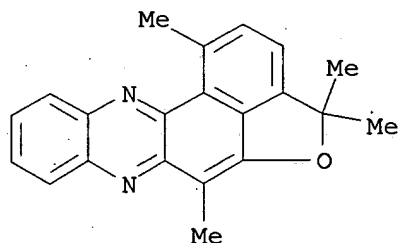
AB Oxygenation of cadalene (I, R=R1=Me) in DMSO or DMF at 120° for 30
 h yielded I (R = CH2OH, CHO, R1 = Me; R = Me, R1 = CHO), quinone II, and
 naphthofuran III. Similar oxidation of eudalene (IV, R2 = Me, R3 = CHMe2)
 gave IV (R2 = Me, CH2OH, CHO, R3 = CHMe2; R2 = Me, R3 = Ac).

IT 10124-06-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

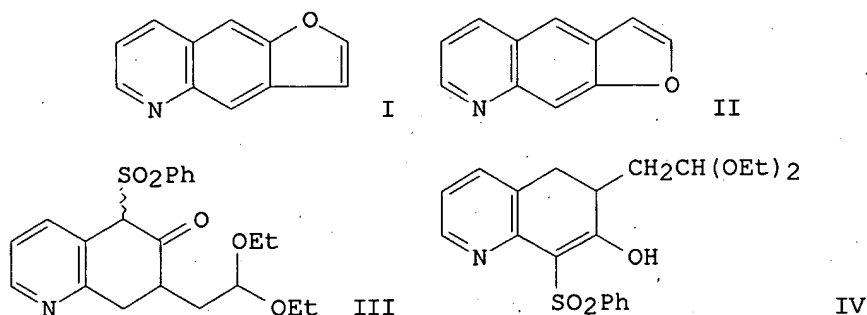
RN 10124-06-8 CAPLUS

CN 4H-Isobenzofuro[7,1-ab]phenazine, 1,4,4,6-tetramethyl- (7CI, 8CI, 9CI)
 (CA INDEX NAME)



L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
 1983:125923 Document No. 98:125923 Versatile syntheses of quinolines by
 annulation of pyridines. Synthesis of furo[2,3-g]- and
 -[3,2-g]quinolines. Ghera, E.; Ben-David, Y.; Rapoport, H. (Dep. Org.
 Chem., Weizmann Inst. Sci., Rehovot, Israel). Journal of Organic
 Chemistry, 48(6), 774-9 (English) 1983. CODEN: JOCEAH. ISSN: 0022-3263.
 OTHER SOURCES: CASREACT 98:125923.

GI



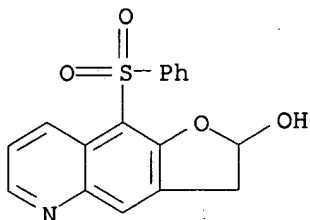
AB A new, versatile annulation route for the synthesis of substituted
 quinolines has been developed by using regioisomeric bifunctional pyridine
 derivs. with vicinal bromomethyl and (phenylsulfonyl)methyl groups. The
 sequence consists of (a) alkylation of substituted di-Et malonates with
 these bromomethylpyridines and (b) intramol. acylation with concomitant
 decarboxylation and leads to quinoline derivs. variously substituted in
 the carbocycle. A simultaneous desulfurization-aromatization of the
 carbocycle has been developed for these cyclized sulfones.
 5-(Phenylsulfonyl)-7-allyl-6-quinolinol, obtained via this cyclization and
 dehydrogenation, was then used for the preparation of furo[2,3-g]quinoline
 derivs. The novel parent systems furo[2,3-g]- and -[3,2-g]quinoline (I
 and II) were obtained in good yield in a one-operation acid-induced
 cyclization-elimination sequence from the bicyclic annulation products III
 and IV, resp.

IT 84583-45-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and dehydration of)

RN 84583-45-9 CAPLUS

CN Furo[2,3-g]quinolin-2-ol, 2,3-dihydro-9-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

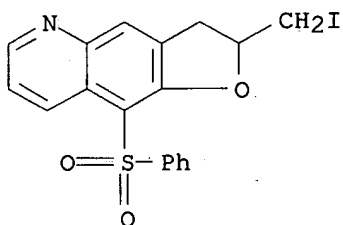


IT 84583-48-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and dehydroiodination of)

RN 84583-48-2 CAPLUS

CN Furo[2,3-g]quinoline, 2,3-dihydro-2-(iodomethyl)-9-(phenylsulfonyl)- (9CI)
(CA INDEX NAME)



L6 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

1968:114314 Document No. 68:114314 Contribution to the chemistry of perezine. Joseph-Nathan, Pedro; Reyes, J.; Gonzalez, Maria P. (Inst. Politec. Nac. Mexico City, Mexico City, Mex.). Tetrahedron, 24(10), 4007-13 (English) 1968. CODEN: TETRAB. ISSN: 0040-4020.

GI For diagram(s), see printed CA Issue.

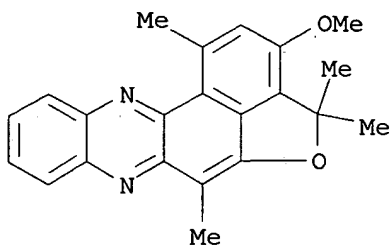
AB The sequence of reactions described confirms that perezine (I) is a quinone methide related to the 2H-naphtho[1,8-bc]furan system. The structures of two oxidation derivs. isolated earlier are established.

IT 18142-22-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 18142-22-8 CAPLUS

CN 4H-Isobenzofuro[7,1-ab]phenazine, 3-methoxy-1,4,4,6-tetramethyl- (8CI, 9CI) (CA INDEX NAME)



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LOGOFF? (Y)/N/HOLD:.

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ENTRY	SESSION
31.02	179.99

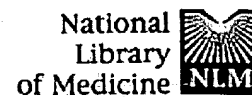
FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-3.91	-3.91

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STN INTERNATIONAL LOGOFF AT 11:09:58 ON 05 AUG 2003

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Lipid peroxidation in human proteinuric disease.

Solin ML, Ahola H, Haltia A, Ursini F, Montine T, Roveri A, Kerjaschki Holthofer H.

The Haartman Institute, Division of Bacteriology and Immunology, University of Helsinki, Helsinki, Finland.

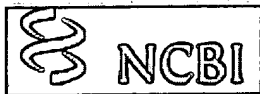
BACKGROUND: While metabolically generated oxidants are produced locally in experimental glomerular diseases, little is still known of their significance and respective scavenger systems in human glomerular diseases. **METHODS:** We studied kidneys from patients with congenital nephrotic syndrome of the Finnish type (CNF), a human model disease of isolated proteinuria. Expression of specific mRNAs for a major antioxidant system against lipoperoxidation [phospholipid hydroperoxide glutathione peroxidase (PHGPx)] and for mitochondrial proteins were studied in Northern blotting together with analysis of PHGPx in semiquantitative reverse transcription-polymerase chain reaction (RT-PCR). The respective proteins and lipoperoxide (LPO) adducts malonyldialdehyde (MDA) and 4-hydroxynonenal (4-HNE) were analyzed in immunohistochemistry. **RESULTS:** PHGPx and the mitochondrially encoded subunits of cytochrome oxidase were distinctly down-regulated within the glomeruli of CNF kidneys. These changes were confirmed in semiquantitative RT-PCR. Increases of lipoperoxidation products MDA and 4-HNE were constantly found in the glomeruli of CNF. In agreement with findings in CNF, similar results were obtained in biopsies from other human glomerular diseases. **CONCLUSION:** These findings suggest that local mitochondrial damage initiates LPO, which causes deposition of the cytotoxic LPO products in glomeruli, as seen especially in CNF kidneys. Together with down-regulation of the local antioxidant protection, these may be important pathophysiologic mechanisms in human glomerular disease.

PMID: 11168930 [PubMed - indexed for MEDLINE]



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Edaravone Mitsubishi-Tokyo.

Tabrizchi R.

Memorial University of Newfoundland, Faculty of Medicine, Basic Medical Sciences, Health Sciences Centre, St John's, NF, A1B 3V6, Canada.

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Mitsubishi-Tokyo (formerly Mitsubishi Chemical) is developing edaravone (norphenazone), a free radical scavenger, for the potential treatment of cardiovascular disease, cerebrovascular ischemia and cerebral edema. By Feb 2000, edaravone had been filed in Japan for the treatment of acute brain infar and was in phase III trials for subarachnoid hemorrhage [365460]. The comp blocks the action of the lipoperoxide, 15-HPETE, which normally increases age and may be associated with neurodegeneration.

Publication Types:

- Review
- Review, Tutorial

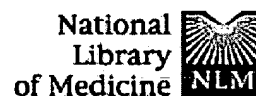
PMID: 11249718 [PubMed - indexed for MEDLINE]



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Combination of a calcium antagonist, a lipid-peroxidation inhibitor and an angiotensin AT1-receptor antagonist provides additive myocardial infarct size-limiting effect in pigs.

Shimizu M, Wang QD, Sjoquist PO, Ryden L.

Department of Cardiology, Karolinska Hospital, Stockholm, Sweden.

The calcium antagonist felodipine, the lipid-peroxidation inhibitor H290/51, the angiotensin II type 1 (AT1)-receptor antagonist candesartan all exert beneficial effects on myocardial ischemia/reperfusion injury. This study was undertaken to test the hypothesis that a combination of these drugs with different pharmacological properties could exert additive cardioprotective effects. Anesthetized pigs were subjected to 45 min of left anterior descending coronary artery occlusion followed by 240 min of reperfusion. Five groups of pigs were randomly given either 0 microM (7 nmol/kg) felodipine, 1.0 microM (3.1 microg/kg) H 290/51, 4.2 microM (20 microg/kg) candesartan, a cocktail of these three drugs, or vehicle (n = 6 for each) for 30 min starting at 5 min before reperfusion by coronary venous retroinfusion, which delivers drugs specifically to the ischemic regions. Systolic segment shortening (%SS) was measured by sonomicrometer. The myocardium at risk and the final infarct size were determined by Evans blue and 2,3,5-triphenyltetrazolium chloride staining. The hemodynamics did not change significantly during the study. In the vehicle group, the recovery of coronary flow was not maintained during reperfusion, and it was significantly lower after 240 min of reperfusion than during the preischemic period ($p < 0.05$). The coronary flow in the drug-treated groups was approximately the same by the end of the reperfusion period as that before the induction of ischemia. In the ischemic myocardium, slightly recovered during reperfusion in the four drug-treated groups, but not in the vehicle group. The infarct size, expressed as a percentage of the myocardium at risk, was smaller in all four drug-treated groups compared with the vehicle group. The infarct size in the cocktail group was significantly smaller than that in the groups given felodipine, H290/51, or candesartan alone. These results demonstrate that a combination of a calcium antagonist, a lipid-peroxidation inhibitor, and an angiotensin AT1-receptor antagonist has an additive effect on infarct limitation, indicating that combined therapy with agents having different pharmacological modes of action may provide better cardioprotection than any of the drugs alone. The findings also support the view that reperfusion injury is possibly mediated

a combination of mechanisms.

PMID: 10511125 [PubMed - indexed for MEDLINE]

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Efficacy and mechanisms of action of the cytoprotective lipid peroxidation inhibitor tirilazad mesylate in subarachnoid haemorrhage.

Hall ED.

CNS Diseases Research, Pharmacia & Upjohn, Inc., Kalamazoo, Michigan 4 USA.

Subarachnoid haemorrhage (SAH) following cerebral aneurysm rupture or trauma can result in the induction of secondary ischaemic brain damage via a decrease in microvascular perfusion, a disruption of the blood-brain barrier and consequent vasogenic oedema, and the delayed spasm of the major cerebral arteries (i.e. vasospasm). It is increasingly apparent that oxygen radical-induced, iron-catalysed lipid peroxidation (LP) within the subarachnoid blood and vascular wall play a key role in the occurrence of these secondary events. Tirilazad mesylate is a cytoprotective inhibitor of LP that works by a combination of radical scavenging and membrane stabilizing properties. It has been demonstrated to attenuate the acute and delayed vascular consequences of SAH and to protect the brain against ischaemic insults. Much of its action is mediated by an effect on the vascular endothelium, although it also appears to exert some direct neuroprotection and inhibit LP in the subarachnoid blood. These actions of tirilazad in experimental SAH are reviewed.

Publication Types:

- Review
- Review, Tutorial

PMID: 8737119 [PubMed - indexed for MEDLINE]

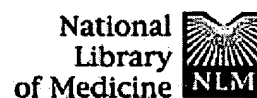


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Aminosteroids for acute traumatic brain injury.

Roberts I.

Department of Epidemiology, Institute of Child Health, 30 Guilford Street, London, UK, WC1N 1EH. Ian.roberts@ich.ucl.ac.uk

BACKGROUND: Traumatic brain injury is a leading cause of premature death and disability. Post-traumatic membrane lipid peroxidation has been proposed as one mechanism leading to secondary brain damage following head injury. Aminosteroids have been shown to inhibit lipid peroxidation in laboratory animals and have the potential to improve outcome following head injury. **OBJECTIVE:** To quantify the effectiveness and safety of aminosteroids in the treatment of traumatic brain injury. **SEARCH STRATEGY:** We searched the Cochrane In-Group trials register, The Cochrane Controlled Trials Register, MEDLINE and EMBASE. We contacted experts in the field and the company that manufacture tirilazad. **SELECTION CRITERIA:** We sought to identify all randomised controlled trials of aminosteroids versus placebo in the treatment of acute traumatic brain injury. Studies using a quasi random form of allocation, such as alternation, were excluded from the review. **DATA COLLECTION AND ANALYSIS:** One reviewer examined the electronic search results for reports possibly relevant trials for retrieval in full. Two reviewers (IR and PA) applied selection criteria independently to the trial report, with no disagreement. **MAIN RESULTS:** Two randomised controlled trials have examined the effect of the aminosteroid tirilazad mesylate on death and disability following head injury. In total, only the results of one of these trials are available for analysis. The risk of death in patients treated with tirilazad was almost identical to those given placebo (RR=1.05 (95% confidence interval 0.86 to 1.29)). The risk of death and severe disability in patients treated with tirilazad was again almost identical to those given placebo (RR=1.07 (95% confidence interval 0.93 to 1.23)). **REVIEWER CONCLUSIONS:** There is no evidence to support the routine use of aminosteroids in the management of traumatic head injury. On the basis of the existing evidence from randomised trials of aminosteroids in head injury it is not possible to rule out the possibility of moderate but potentially clinically important benefits or harms. Further randomised controlled trial of tirilazad mesylate with 1156 participants has been completed, the results of which should become available in the near future.

Publication Types:

- Review
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PMID: 11034722 [PubMed - indexed for MEDLINE]

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